REMARKS

Applicant acknowledges, with thanks, the withdrawal of the objections to the drawings and the legends.

The Examiner withdrew claims 32-36 from consideration in part regarding SEQ ID NO. 4, 6, and 8. As amended, claim 32 is now only directed to amino acids 150-411 of SEQ ID NO. 2. Applicant notes that the Office Action mailed May 20, 2003 acknowledges Applicant's claim for priority based on Canadian Patent No. 2, 230,991, filed May 11, 1998. Specifically, the 262 amino acid translation product, representing amino acids 150-411 of SEQ ID NO. 2, finds full support in Figure 4 of Canadian Patent No. 2, 230, 991. Consequently, the claims are entitled to the benefit of the May 11, 1998 filing date of the priority application, which effective filing date is earlier than the cited registration of a corresponding nucleic acid sequence on October 28, 1998 under the nucleotide accession number AF072242.

As amended, claim 32 is directed to "a method for altering the methylation activity of DNA demethylase comprising amino acids 150-411 of SEQ ID NO.2" by inhibiting the DNA demethylase with certain inhibitors. Applicant respectfully notes claim 32 is directed to subject matter that is **within the scope of the originally elected group of claims**. In Applicant's response, dated February 19, 2003, Applicant elected Group XIII-2. Group XIII-2 was identified in the Office Action dated October 17, 2002, as:

> Claims 19-22 (partially), and 23-25, drawn to the use of an antagonist or inhibitor of the human DNA demethylase of SEQ ID NOs. 2 and 4, for restoring an aberrant methylation pattern in a patient DNA, or for changing a methylation pattern in the patient DNA.

Rejection Under 35 U.S.C. 112, second paragraph

The indefiniteness rejection of claim 32 based on the phrase "wherein production of DNA demethylase is increased in comparison with that of a non-tumor cell" has been rendered moot by deletion of this phrase from the claim.

Rejections Under 35 U.S.C. 112, first paragraph

Written Description

Claims 32-36 were rejected as failing to comply with the written description requirement. The Office Action states that the claims are directed to a method for inhibiting tumorigenesis by altering methylation pattern *in vivo*, but that tumorigenesis is generic and encompasses many phenomena related to the onset of carcinogenic transformation and progression of tumor. The Office Action also alleges that the application is silent as to the methylation pattern of any gene in any patient. As now amended, claim 32 no longer refers to tumorigenesis or methylation pattern.

Claim 32 recites generally a method of inhibiting DNA demethylase activity. The enzymatic methylation activity of DNA demethylase finds support throughout the description and most notably at pages 22-34 of the description. Human embryonal kidney cells, transfected with dMTase cDNA also showed demethylation activity as disclosed in pages 39-42 of the description. Inhibition of the methylation activity of dMTase finds support at page 43 of the description and at Figures 14-16. In fact, the Office Action dated May 20, 2003 notes that the application contains allowable subject matter and acknowledges that the Applicants were the first to discover human DNA demethylase consisting of amino acid residues 150-411 of SEQ ID NO. 2 and encoding DNA and that the Applicants also were the first who demonstrated its function by presenting the details of the enzymatic reaction. Applicant wishes to specifically note that Hendrich et al.'s disclosure of SEQ ID NO:2 on October 28, 1998 is not prior art with respect to the present application because it is subsequent to Applicant's Canadian priority Application No. 2, 230, 991, filed May 11, 1998, which fully discloses this sequence.

The rejection was also based, in part, on claim 32 allegedly embracing the use of any antagonist or inhibitor of DNA demethylase and on the terms antagonist or inhibitor being generic terms. As amended, claim 32 is now directed to the use of the following specific groups of inhibitors: double stranded $C^{m}G$ oligonucleotides,

anti-DNA demethylase antibodies, antisense oligonucleotides of DNA demethylase, imidazole and derivatives of imidazole.

The Office Action raises a question whether the structure of the antisense oligonucleotide of DNA demethylase is described in detail because the antisense vector of Fig. 15 is depicted schematically. The Applicant respectfully submits that the anti-sense sequence is fully disclosed to persons of skill in the art. The sense sequence of DNA demethylase is explicitly disclosed as SEQ ID NO. 1. Specifically, nucleotides 540-1325 of SEQ ID NO. 1 corresponds to amino acids 150-411 of SEQ ID NO. 2. As an antisense sequence can be explicitly deduced from the corresponding sense sequence, the disclosure of the sense sequence thus also constitutes a disclosure of the anti-sense sequence. Furthermore, the context within which the antisense sequence is used is specifically disclosed as the elements of the vector are explicitly shown in Figure 15.

Applicant therefore respectfully submits that amended claim 32 and previously presented claims 33 and 34, dependent thereon, satisfy the written description requirement in full compliance with the requirements of the first paragraph of 35 U.S.C. §112.

Claims 35 and 36 have been canceled, and the rejection of claim 36 as failing the written description requirement, has been thereby rendered moot.

New claims 41-44 are submitted for consideration. Each of claims 41-44 is dependent from amended claim 32 and is directed to each specific genus of inhibitor recited in amended claim 32.

Scope of Enablement

Claims 32-36 also were rejected as not providing enablement for the inhibition of tumorigenesis in vivo. As amended, claim 32 is no longer directed to a method for inhibiting tumorigenesis. Amended claim 32 is directed to a method for inhibiting the methylation activity of DNA demethylase.

Claims 32-36 were additionally rejected as not providing enablement for the inhibition by any inhibitor of dMTase. As mentioned above, amended claim 32 recites the following specific genus of inhibitors: double stranded $C^{m}G$ oligonucleotides, anti-DNA demethylase antibodies, antisense oligonucleotides of DNA demethylase, imidazole and derivatives of imidazole. The Final Office Action specifically states at page 10 that the specification is enabling for meCpG, imidazole and dMTase antibodies. The Applicant therefore respectfully submits that any rejection in this regard is effectively overcome.

The remaining rejections regarding enablement are founded on the previous claims being directed to methods of inhibition of tumorigenesis and the alteration of methylation pattern to silence a gene. As discussed above, the amended claims no longer recite inhibition of tumorigenesis, methylation patterns or the silencing of genes. Applicant thus respectfully submits that, as amended, the claims of the application are properly enabled by the specification.

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application is general, the Examiner is respectfully requested to telephone the undersigned at (202) 624-2845 so that any such questions can be expeditiously resolved.

If necessary, this document should be construed as a Petition for an extension of time sufficient to enable a timely response, and the Commissioner is hereby authorized to charge any needed fee to deposit account #05-1323 (Ref. 038630.48896US).

Respectfully submitted,

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